

January 12, 1970

Dr. Arthur J. Tamplin

Dear Dr. Tamplin,

Thank you very much for sending me your AAAS paper and for the copy of the Meyer et al. 1969.

I am afraid that my critical remarks are going to sound like quibbling especially as I am in complete accord with your main recommendations. However, I have to put the burden of my argument on the rather weaker foundation of our unresolved ignorance, for I must admit to significant loopholes in the rigor of your arguments about "doubling dose" and in the Johns Hopkins epidemiological study. The latter is inherently faulty for its failure to do, what may be impossible, a sufficient matching of the economic and health-social status of the exposed compared to the controlled group. On the face of it there is grave suspicion of this fault from the difference in reproductive performance. The method used by the Johns Hopkins group was extremely crude, relying upon the categorization of the senses tract of residents only! It would be very desirable if the controlled cohort could be made up of siblings of the exposed women. I have also deterred by the purely theoretical difficulty but I find it rather implausible that there should be an excess of males as the outcome of female germ line irradiation. I will very gladly eat my words if a demonstrated excess of chromosome anomaly is found in this group!

I am afraid I also retain some reservations about the study on pre-natal induction of leukemia on essentially similar grounds. Women who managed to receive such radiation may well be atypical in many other respects including exposure to drugs, dietary habits, the possibility of their own mosaicism for chromosome anomaly, and many other factors. I am just now discussing a protocol for a local study on correlation between x-ray exposure and cigarette smoking. The effects that have been reported appear, frankly, to be rather large in relation to the doses used and furthermore have yet to be related quantitatively to the dose received.

I also have serious questions about the concept of a doubling dose of radiation when this is applied to the prospective incidence of tumors known to be influenced primarily by other carcinogens, for example smoking. I must, of course, admit to the possibility of some interaction or even synergism between radiation and smoking but this is, of course, entirely conjectural at present. I would think the most appropriate

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ANTHONY J. TAMPLIN

way to extrapolate the findings on analyzed forms of cancer would be in terms of absolute yield per unit radiation dose rather than the proportionate increases in regionally typical forms of cancer. However, the interaction of radiation with other environmental factors is of the utmost importance and my argument is not intended to condone an optimistic policy.

This suggests the desirability of some direct studies on fetal cell material to test the hypothesis that the enzymes for repair of DNA damage may be relatively deficient in some immature cell lines. The hypothesis of repair of radiation lesions is scarcely any basis for optimism since most of our measurements are done on material which has had ample latitude for conducting such repair. I would then be deeply concerned about idiosyncratic individuals or special stages of lives or the impact of other environmental factors that may dampen this process.

I would be very grateful if I could have copies of the handbook mentioned in your article relating radionuclides to radiation exposure. I have painfully tried to make a few such calculations myself and would be very pleased to be spared having to make further efforts of this kind. You might also save me considerable effort if you could pass on the references, which I am sure you may have at your fingertips, on explicit studies of the biological consequences of radio-iodine and -crypton.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

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